

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
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# PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 630666.00077		Date of mailing (day/month/year) <b>16 SEP 2005</b> <b>FOR FURTHER ACTION</b> See paragraph 2 below
International application No. PCT/US05/10291	International filing date (day/month/year) 28 March 2005 (28.03.2005)	Priority date (day/month/year) 29 March 2004 (29.03.2004)
International Patent Classification (IPC) or both national classification and IPC IPC(7): A 01N 63/00; A61K 48/00 and US Cl.: 424/93.2, 93.21		
Applicant MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH		

1. This opinion contains indications relating to the following items:

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application  |

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Q. Janice Li, M.D. Telephone No. 703-308-0196
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International application No.

PCT/US05/10291

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-17</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-17</u>	NO
Industrial applicability (IA)	Claims <u>1-17</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-17 lack an inventive step under PCT Article 33(3) as being obvious over Alisky in view of Phelps et al.

The claims are drawn to a method of treating a patient comprising implanting into the patient a porcine heart valve from a porcine tissue, wherein the cells of the porcine tissue have reduced or undetectable expression of Gal1,3-GT, obtained from a pig whose genome comprises a disruption of the Gal1,3-GT gene. The claims are also drawn to manufactured heart valve used for the implantation, and method of manufacture.

Although the cited references do not actually making a commercial product of the claimed pig heart valve or implanting such in a patient, Phelps et al reported successful production of pigs whose genome comprises a homozygous disruption of the Gal1,3-GT gene, and whose cells lack detectable level of Gal1,3-GT. Alisky clearly teaches the intended use of the pig produced by Phelps et al for treating human patients in need of. Accordingly, it would have been obvious to the skilled in the art to use the pigs produced by Phelps et al for manufacture heart valves for transplantation. Thus, the claimed invention as a whole was prima facie obvious.

Claimd 1-17 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.